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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,652	09/05/2000	Lie-Fen Shyur	4910-8	7362

7590 07/12/2005

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,652	SHYUR ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-21,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-21 and 25-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The after final amendment filed on April 20, 2005, amending claims 20-21, canceling claims 23-24 and adding claims 25-26, has been entered.

Claims 8-21 and 25-26 are pending. Claims 8-19 are withdrawn. Claims 20-21 and 25-26 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on April 20, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Applicants have stated that the Examiner has rejected all claims when some claims were advised as allowable. Amendments to the claims and reconsideration of the claims prompted the rejections in the previous office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 and claims 21 and 25-26 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the phrase "isolated truncated glucanase that contains an amino acid sequence". The phrase is not clear to the Examiner because a protein does not "contain" an amino acid sequence but "consists of" or "comprises" an amino acid sequence.

Claim 20 and claims 21 and 25-26 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the phrase "said amino acid sequence comprises SEQ ID NO:1". It is not clear to the Examiner if a truncated glucanase having a total 267 amino acids has an extension at N-terminal or C-terminal or at both termini. Examiner has interpreted the phrase broadly to encompass a truncated glucanase comprising SEQ ID NO:1 and an extension at the N-terminus, C-terminus or at both termini.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the phrase "absent a SEQ ID NO:11 segment". It is not clear to the Examiner if the truncated glucanase "absent a SEQ ID NO:11 segment" is a deletion, variant, and whether the glucanase continues to have enzymatic activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20-21 are drawn to truncated glucanases having specific activities of 7499 to 8321 U/mg. However, the truncated glucanases having specific activities of 7499 to 8321 U/mg were not described in the application or claims as originally filed. The specification as filed does contain disclosure of some specific activities of truncated glucanases, but not the range as currently recited in the claim 20, specific activities of 7499 to 8321 U/mg. Therefore, claims 20-21 contain new matter.

Given this lack of description of truncated glucanases having specific activities of 7499 to 8321 U/mg, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 20-21 at the time of filing of the instant application.

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (See rejection of the phrase "said amino acid sequence comprises SEQ ID NO:1" under 35 U.S.C. 112, 2nd paragraph above).

Claims 20-21 are drawn to truncated glucanases having enhanced glucanase activity relative to the wild type glucanase, wherein said truncated glucanases consist of 248-267 amino acids and wherein said truncated glucanases comprises SEQ ID NO:1 or comprises SEQ ID NO:1 with a C-terminal extension of 1 to 19 amino acids. Therefore, the claims are drawn to a genus of glucanase variants having any structure comprising SEQ ID NO:1 with N-terminal or C-terminal extension of 1 to 19 amino acids, wherein the extension comprises of any amino acids. The specification only teaches two species, truncated glucanase of SEQ ID NOs: 1 and 2 having enhanced enzymatic activity. Two species are not enough to describe the whole genus. The specification does not describe the structure of all variants that are encompassed in the genus nor describe which residues can be added to the N-terminus or C-terminus of SEQ ID NO:1 to impart the mutant with enhanced glucanase activity. Therefore, the specification fails to describe the structure of all variants of the glucanase of SEQ ID NO:1 comprising any C-terminal extension of 1-19 amino acids.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention

in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 20-21.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that claims 20-21 and 25-26 have been amended to recite the activity and thermal tolerance and since the specification discloses how to make truncated glucanase by exemplifying the two species of SEQ ID NO1 and 2, the claims meet the written description requirement. Examiner respectfully disagrees. (Examiner notes that claims 25-26 have not been rejected for lack of written description, only claims 20-21 have been rejected.) As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., **structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.** A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in

possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species, cannot be achieved by disclosing only two species within the genus. In the instant case the claimed genera of claims 20-21 include species which are widely variant in structure. As such, the description of solely functional features present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus.

Hence the rejection is maintained.

Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the glucanase of SEQ ID NOs: 1 and 2, does not reasonably provide enablement for SEQ ID NO:1 having a N-terminal, C-terminal or both N-terminal and C-terminal extension comprising any amino acid residues. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 20-21 are drawn to truncated glucanases having enhanced glucanase activity relative to the wild type glucanase, wherein said truncated glucanases consist of 248-267 amino acids and wherein said truncated glucanases comprise SEQ ID NO:1 or comprises SEQ ID NO:1 with a C-terminal extension of 1 to 19 amino acids. Therefore, the claim encompasses any variants and mutants of the glucanase of SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of glucanase variants and mutants, broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a glucanase having the amino acid sequence of SEQ ID NOs:1 and 2. It would require undue experimentation of the skilled artisan to make and use the claimed variants and mutants of SEQ ID NO:1. The specification is limited to teaching the use of a glucanase of SEQ ID NO:2 but provides no guidance with regard to the making of

variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all mutants and variants of the glucanase of SEQ ID NO:1, because the specification does not establish: (A) specific amino acid residues which can be safely added to the C-terminus, N-terminus or both termini of SEQ ID NO:1 and result in a glucanase having enhanced glucanase activity; (B) the general tolerance of the glucanase of SEQ ID NO:1 to such modification and extent of such tolerance; (C) a rational and predictable scheme for adding any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides

insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any variants and mutants of the glucanase of SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any mutants and variants of the glucanase of SEQ ID NO:1 having enhanced glucanase activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that claims 20-21 have been amended to recite the activity and thermal tolerance and since the specification discloses how to make truncated glucanase, the claims meet the enablement requirement. While that may be so, those limitations alone do not overcome enablement requirements. Examiner respectfully disagrees because the claims are drawn to truncated glucanase comprising SEQ ID NO:1 and any amino acids, attached to the N-terminus, C-terminus and at both termini. The specification only teaches two examples of a truncated glucanase having the

recited activity and thermal tolerance, SEQ ID NOs:1-2. Also, the specification fails to teach adding amino acids to the N-terminus of SEQ ID NO:1 or to both termini.

Applicants also argue that there is no need for undue experimentation, let alone "essentially infinite choices". Examiner respectfully disagrees. As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity or in the instant case, enhanced glucanase activity and increased thermal tolerance. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation for adding up to 19 amino acids to the C-terminus.

Applicants argue that claims 20-21 and 25-26 recite desired properties and therefore are enabled by the original specification by discussing two cases cited by MPEP 2164.06(b). Examiner respectfully disagrees. MPEP 2164.06(b) states "The following summaries should not be relied on to support a case of lack of enablement without carefully reading the case" before discussion of *In re Wands* and *In re Bundy*. It appears Applicants have not compared the claims and fact patterns involved in the two case.

In *In re Wands*, claims were drawn to making monoclonal antibodies with desired characteristics. The instant claims are drawn to making mutants and variants of a

truncated enzyme with desired characteristics. The level of skill, knowledge in the art and experimentation in making antibodies and making variants of an enzyme having increased enzymatic activity and thermal tolerance are not analogous.

In *In re Bundy*, the courts found that the disclosure was sufficient to enable one skilled in the art to use the claimed analogs of naturally occurring prostaglandins even though the specification lacked any examples of specific dosages. In the instant case, the claims are not rejected for lack of examples of specific dosages but for lacking enablement for making truncated glucanase comprising any amino acids attached at the C-terminus, N-terminus or at both termini of SEQ ID NO:1. The level of skill, knowledge in the art and experimentation in using therapeutics lacking examples of its dosages and making variants of an enzyme having increased enzymatic activity and thermal tolerance are not analogous.

Applicants also argue that the quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make the use the invention, that extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance and that even if one or ordinary skill in the art would need to do some experimentation, he or she would only engage in routine experimentation. Examiner respectfully disagrees and asserts that in order to make variants as claimed a skilled artisan needs given sufficient direction or guidance and more than that for routine experimentation. As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific

knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity or in the instant case, enhanced glucanase activity and increased thermal tolerance. It is this specific guidance of adding specific amino acids to the C-terminus that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation.

Hence the rejection is maintained.

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Patent Examiner 1652